

AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions and listings of claims in the application.

LISTING OF CLAIMS

1-79. (Canceled).

80. (New) A method for classifying a patient having diffuse large B-cell lymphoma (DLBCL), the method comprising:

measuring expression of a plurality of genes in a tumor sample from the patient to produce measured expression values;

normalizing said measured expression values to produce normalized expression values;

correlating said normalized expression values to normalized reference expression values obtained for said plurality of genes from DLBCL patients grouped into classification groups; and

classifying the patient into one of said classification groups based upon weighed predictor Z in formula:

$$Z = (A \times LMO2) + (B \times BCL6) + (C \times FN1) + (D \times CCND2) + (E \times SCYA3) \\ + (F \times BCL2)$$

wherein A is -0.03, B is -0.2, C is -0.2, D is 0.03, E is 0.2, and F is 0.6 and wherein LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2 are log base 2 of normalized expression values for genes LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2, respectively.

81. (New) The method according to claim 80 wherein a Z value of less than -0.06 indicates high probability of survival, a Z value of from -0.06 to 0.09 indicates medium probability of survival and a Z value of greater than 0.09 indicates low probability of survival.

82. (New) The method according to claim 80, further comprising:
predicting survival of the patient wherein said plurality of genes are predictive of probability of survival and wherein said classification groups comprise groups of said DLBCL patients having known overall probability of survival.

83. (New) The method according to claim 82 wherein said known overall probability of survival comprises overall probability of survival after anthracycline-based chemotherapy.

84. (New) The method according to claim 80 wherein said normalized expression values comprise ratios of measured expression values obtained from said plurality of genes to expression values of a housekeeping gene.

85. (New) The method according to claim 84 wherein the housekeeping gene is *PGK1* or *GAPDH*.

86. (New) The method according to claim 80 wherein said measuring expression of said plurality of genes in said tumor sample from the patient comprises performing real time RT-PCR on a portion of said tumor sample from the patient.

87. (New) The method according to claim 80, further comprising:
determining whether said normalized expression values are similar to said normalized reference expression values obtained for said plurality of genes grouped into said classification groups selected from low, medium and high overall probability of survival after anthracycline-based chemotherapy.

88. (New) The method according to claim 80 wherein said plurality of genes is selected from the group consisting essentially of LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2.

89. (New) The method according to claim 80 wherein said plurality of genes comprises LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2.

90. (New) The method according to Claim 80 wherein said measuring expression of a plurality of genes comprises:

hybridizing a plurality of primers to said plurality of genes, said plurality of primers being selected from a group consisting essentially of SEQ. ID. NO. 11, SEQ. ID. NO. 12, SEQ. ID. NO. 20, SEQ. ID. NO. 21, SEQ. ID. NO. 26, SEQ. ID. NO. 27, SEQ. ID. NO. 50, SEQ. ID. NO. 51, SEQ. ID. NO. 62, SEQ. ID. NO. 63, SEQ. ID. NO. 104, and SEQ. ID. NO. 105.

91. (New) A method for determining a probability of survival of a patient diagnosed with DLBCL, the method comprising:

amplifying a plurality of genes using a plurality of primers designed to hybridize to said plurality of genes, said plurality of primers are selected from a group consisting essentially of SEQ. ID. NO. 11, SEQ. ID. NO. 12, SEQ. ID. NO. 20, SEQ. ID. NO. 21, SEQ. ID. NO. 26, SEQ. ID. NO. 27, SEQ. ID. NO. 50, SEQ. ID. NO. 51, SEQ. ID. NO. 62, SEQ. ID. NO. 63, SEQ. ID. NO. 104, and SEQ. ID. NO. 105;

measuring expression of said plurality of genes;

normalizing said expression to produce normalized expression values; and

correlating said normalized expression values to data organized into classification groups to determine the probability of survival of the patient diagnosed with DLBCL.

92. (New) The method according to claim 91 wherein said correlating said normalized expression values are based upon weighed predictor Z in formula:

$$Z = (A \times LMO2) + (B \times BCL6) + (C \times FN1) + (D \times CCND2) + (E \times SCYA3) \\ + (F \times BLC2)$$

wherein A is -0.03, B is -0.2, C is -0.2, D is 0.03, E is 0.2, and F is 0.6 and wherein LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2 are log base 2 of normalized expression values for genes LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2, respectively.

93. (New) The method according to claim 92 wherein a Z value of less than -0.06 indicates high probability of survival, a Z value of from -0.06 to 0.09 indicates medium probability of survival and a Z value of greater than 0.09 indicates low probability of survival.

94. (New) The method according to claim 91 wherein said correlating said normalized expression values are based upon weighed predictor Z in formula:

$$Z = (A \times LMO2) + (B \times BCL6) + (C \times FN1) + (D \times CCND2) + (E \times SCYA3) \\ + (F \times BLC2)$$

wherein A is -0.0273, B is -0.2103, C is -0.1878, D is 0.0346, E is 0.1888 and F is 0.5527 and wherein LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2 are log base 2 of normalized expression values for genes LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2, respectively.

95. (New) The method according to claim 94 wherein a Z value of less than 0.063 indicates high probability of survival, a Z value of from -0.063 to 0.093 indicates medium probability of survival and a Z value of greater than 0.093 indicates low probability of survival.

96. (New) The method according to claim 91, further comprising:
predicting survival of the patient wherein said plurality of genes are predictive of probability of survival and wherein said classification groups comprise groups of said DLBCL patients having known overall probability of survival.

97. (New) The method according to claim 96 wherein said known overall probability of survival comprises overall probability of survival after anthracycline-based chemotherapy.

98. (New) The method according to claim 91 wherein said classification groups selected from low, medium and high overall probability of survival after anthracycline-based chemotherapy.

99. (New) The method according to claim 91 further comprising performing reverse transcriptase on mRNA from a tumor sample from the patient.

100. (New) The method according to claim 91 wherein said data organized in classification groups comprises normalized expression data of said plurality of genes collected from DLBCL patients with a known survival rate.

101. (New) The method according to claim 91, wherein said plurality of genes is selected from the group consisting essentially of LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2.

102. (New) The method according to claim 105, further comprising detecting a probe, said probe is selected from the group consisting essentially of SEQ. ID. NO. 10, SEQ. ID. NO. 19, SEQ. ID. NO. 25, SEQ. ID. NO. 49, SEQ. ID. NO. 91, and SEQ. ID. NO. 103.

103. (New) A method for determining a probability of survival of a patient diagnosed with DLBCL, the method comprising:

amplifying a plurality of primers designed to measure an expression of a plurality of predictive genes in a sample from the patient diagnosed with DLBCL, and producing normalized expression data, said plurality of predictive genes comprise LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2;

providing a database comprising expression data sets from said plurality of predictive genes obtained from DLBCL patients with known survival data; and

correlating said normalized expression data with said expression data sets to determine the probability of survival of the patient diagnosed with DLBCL.

104. (New) The method according to claim 103, further comprising providing a plurality of classification groups grouped from said expression data sets from said plurality of predictive genes obtained from DLBCL patients with known survival data.

105. (New) The method according to claim 103, further comprising classifying said expression data set from said plurality of predictive genes obtained from DLBCL patients with known survival data into a plurality of classification groups that are predictive of a probability of survival.

106. (New) The method according to claim 103 wherein said plurality of predictive genes obtained from DLBCL patients with known survival data comprise LMO2, BCL-6, FN1, CCND2, SCYA3 and BCL-2.

107. (New) The method according to claim 103, further comprising detecting a probe, said is probe selected from the group consisting essentially of SEQ. ID. NO. 10, SEQ. ID. NO. 19, SEQ. ID. NO. 25, SEQ. ID. NO. 49, SEQ. ID. NO. 91, and SEQ. ID. NO. 103.

108. (New) The method according to claim 103, further comprising determining a probability of survival based upon weighed predictor Z in formula:

$$Z = (A \times LMO2) + (B \times BCL6) + (C \times FN1) + (D \times CCND2) + (E \times SCYA3) \\ + (F \times BLC2)$$

wherein A is -0.03, B is -0.2, C is -0.2, D is 0.03, E is 0.2, and F is 0.6 and wherein LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2 are log base 2 of normalized expression values for genes LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2, respectively.

109. (New) The method according to claim 108 wherein a Z value of less than -0.06 indicates high probability of survival, a Z value of from -0.06 to 0.09 indicates medium probability of survival and a Z value of greater than 0.09 indicates low probability of survival.

110. (New) The method according to claim 103 wherein said correlating said normalized expression values are based upon weighed predictor Z in formula:

$$Z = (A \times LMO2) + (B \times BCL6) + (C \times FN1) + (D \times CCND2) + (E \times SCYA3) \\ + (F \times BLC2)$$

wherein A is -0.0273, B is -0.2103, C is -0.1878, D is 0.0346, E is 0.1888 and F is 0.5527 and wherein LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2 are log base 2 of normalized expression values for genes LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2, respectively.

111. (New) The method according to claim 110 wherein a Z value of less than 0.063 indicates high probability of survival, a Z value of from -0.063 to 0.093 indicates medium probability of survival and a Z value of greater than 0.093 indicates low probability of survival.

112. (New) The method according to claim 103 wherein said plurality of primers is selected from the groups consisting essentially of SEQ. ID. NO. 11, SEQ. ID. NO. 12, SEQ. ID. NO. 20, SEQ. ID. NO. 21, SEQ. ID. NO. 26, SEQ. ID. NO. 27, SEQ. ID. NO. 50, SEQ. ID. NO. 51, SEQ. ID. NO. 62, SEQ. ID. NO. 63, SEQ. ID. NO. 104, and SEQ. ID. NO. 105.

113. (New) A method comprising:

providing a plurality of primers designed to hybridize to a plurality of predictive genes in a sample from a patient having DLBCL;

employing real time PCR to measure expression values of said plurality of predictive genes in said sample from the patient having DLBCL to produce measured expression;

providing a database comprising normalized reference expression values of said plurality of predictive genes from a plurality of DLBCL patients having known survival data segregated into a plurality of classification groups having a known probability of survival; and

comparing said measured expression with said normalized reference expression values and outputting a probability of survival based on membership of the patient having DLBCL in one of said plurality of classification groups.

114. (New) The method according to claim 113 wherein said plurality of predictive genes in said sample from the patient having DLBCL is selected from the group consisting essentially of LMO2, BCL-6, FN1, CCND2, SCYA3 and BCL-2.

115. (New) The method according to claim 114, further comprising determining a probability of survival based upon weighed predictor Z in formula:

$$Z = (A \times LMO2) + (B \times BCL6) + (C \times FN1) + (D \times CCND2) + (E \times SCYA3) \\ + (F \times BLC2)$$

wherein A is -0.03, B is -0.2, C is -0.2, D is 0.03, E is 0.2, and F is 0.6 and wherein LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2 are log base 2 of normalized expression values for genes LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2, respectively.

116. (New) The method according to claim 115 wherein a Z value of less than -0.06 indicates high probability of survival, a Z value of from -0.06 to 0.09 indicates medium probability of survival and a Z value of greater than 0.09 indicates low probability of survival.

117. (New) The method according to claim 114 wherein said correlating said normalized expression values are based upon weighed predictor Z in formula:

$$Z = (A \times LMO2) + (B \times BCL6) + (C \times FN1) + (D \times CCND2) + (E \times SCYA3) \\ + (F \times BLC2)$$

wherein A is -0.0273, B is -0.2103, C is -0.1878, D is 0.0346, E is 0.1888 and F is 0.5527 and wherein LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2 are log base 2 of normalized expression values for genes LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2, respectively.

118. (New) The method according to claim 117 wherein a Z value of less than 0.063 indicates high probability of survival, a Z value of from -0.063 to 0.093 indicates medium probability of survival and a Z value of greater than 0.093 indicates low probability of survival.

119. (New) The method according to claim 113 wherein said plurality of predictive genes from said plurality of DLBCL patients having known survival data comprise LMO2, BCL-6, FN1, CCND2, SCYA3 and BCL-2.

120. (New) The method according to claim 113, further comprising normalizing said measured expression values.

121. (New) The method according to claim 113, further comprising calibrating said measured expression values.

122. (New) The method according to claim 113 wherein said plurality of primers is selected from the groups consisting essentially of SEQ. ID. NO. 11, SEQ. ID. NO. 12, SEQ. ID. NO. 20, SEQ. ID. NO. 21, SEQ. ID. NO. 26, SEQ. ID. NO. 27, SEQ. ID. NO. 50, SEQ. ID. NO. 51, SEQ. ID. NO. 62, SEQ. ID. NO. 63, SEQ. ID. NO. 104, and SEQ. ID. NO. 105.

123. (New) The method according to claim 113, further comprising detecting a probe, said probe is selected from the group consisting essentially of SEQ. ID. NO. 10, SEQ. ID. NO. 19, SEQ. ID. NO. 25, SEQ. ID. NO. 49, SEQ. ID. NO. 91, and SEQ. ID. NO. 103.

124. (New) A method for predicting a probability of survival for a patient having DLBCL, the method comprising:

amplifying a plurality of genes predictive of DLBCL from a sample from the patient, said amplifying employing a real time PCR assay comprising a primer set, a probe and a polymerase, said real time PCR assay measuring expression of a plurality of genes predictive of DLBCL in said sample and outputting normalized expression data, said plurality of genes predictive of DLBCL comprise LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2; and

assigning the patient into one of a plurality of classification groups based on said normalized expression data, said plurality of classification groups being representative of a probability of survival of the patient.

125. (New) The method according to claim 124 wherein said assigning is based upon weighed predictor Z in formula:

$$Z = (A \times LMO2) + (B \times BCL6) + (C \times FN1) + (D \times CCND2) + (E \times SCYA3) + (F \times BLC2)$$

wherein A is -0.03, B is -0.2, C is -0.2, D is 0.03, E is 0.2, and F is 0.6 and wherein LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2 are log base 2 of normalized expression values for genes LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2, respectively.

126. (New) The method according to claim 125 wherein a Z value of less than -0.06 indicates high probability of survival, a Z value of from -0.06 to 0.09 indicates medium probability of survival and a Z value of greater than 0.09 indicates low probability of survival.

127. (New) The method according to claim 124 wherein said correlating said normalized expression values are based upon weighed predictor Z in formula:

$$Z = (A \times LMO2) + (B \times BCL6) + (C \times FN1) + (D \times CCND2) + (E \times SCYA3) + (F \times BLC2)$$

wherein A is -0.0273, B is -0.2103, C is -0.1878, D is 0.0346, E is 0.1888 and F is 0.5527 and wherein LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2 are log base 2 of normalized expression values for genes LMO2, BCL6, FN1, CCND2, SCYA3 and BCL2, respectively.

128. (New) The method according to claim 127 wherein a Z value of less than 0.063 indicates high probability of survival, a Z value of from -0.063 to 0.093 indicates medium probability of survival and a Z value of greater than 0.093 indicates low probability of survival.

129. (New) The method according to claim 124, further comprising:
predicting survival of the patient wherein said plurality of genes are predictive of probability of survival and wherein said classification groups comprise groups of said DLBCL patients having known overall probability of survival.

130. (New) The method according to claim 129 wherein said known overall probability of survival comprises overall probability of survival after anthracycline-based chemotherapy.

131. (New) The method according to claim 124 wherein said classification groups selected from low, medium and high overall probability of survival after anthracycline-based chemotherapy.

132. (New) The method according to claim 124, further comprising detecting said probe, said probe is selected from the group consisting essentially of SEQ. ID. NO. 10, SEQ. ID. NO. 19, SEQ. ID. NO. 25, SEQ. ID. NO. 49, SEQ. ID. NO. 91, and SEQ. ID. NO. 103.

133. (New) The method according to claim 124, further comprising providing a database comprising data from said plurality of genes predictive of DLBCL, said data collected from a plurality of DLBCL patients with known survival rates.

134. (New) The method according to claim 133 wherein said database comprising said data is organized into said plurality of classification groups being representative of a probability of survival.

135. (New) The method according to claim 124 wherein said primer set comprises a primer selected from group consisting essentially of SEQ. ID. NO. 11, SEQ. ID. NO. 12, SEQ. ID. NO. 20, SEQ. ID. NO. 21, SEQ. ID. NO. 26, SEQ. ID. NO. 27, SEQ. ID. NO. 50, SEQ. ID. NO. 51, SEQ. ID. NO. 62, SEQ. ID. NO. 63, SEQ. ID. NO. 104, and SEQ. ID. NO. 105.

136. (New) The method according to claim 124 wherein said probe is selected from the group consisting essentially of SEQ. ID. NO. 10, SEQ. ID. NO. 19, SEQ. ID. NO. 25, SEQ. ID. NO. 49, SEQ. ID. NO. 61, and SEQ. ID. NO. 103.